PATHOLOGY OF (MUSTARD?) GAS INHALATION.

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Introduction. The object of this paper is to offer a description of the gross and microscopic pathology produced by the inhalation of (mustard[1]) gas. Of the 37 cases included in this study, 35, according to the field medical cards, were due to mustard gas, 1 to mustard gas and phosgene and 1 to phosgene alone. In 34 cases the action of the gas on the respiratory tract was the main factor in causing death. Two died as a result of extensive skin burns, and 1 of cellulitis of the face and neck following burns in this region. It is evident that though the skin and eyes suffer from contact with this agent, and though death may result from injury in these areas, inhalation and the resulting pathology in the respiratory tract is the important factor in cases which reached this center.

The respiratory tract is attacked from the tip of the epiglottis to the terminal bronchioles and air vesicles. The effects seen here are due (1) to the intense irritation and escharotic action of the gas, and (2) to secondary infection, which promptly occurs. As seen in the autopsy room, more or less of the entire mucosa over this region is covered by a fibrinopurulent exudate, a false membrane, from dirty gray to yellowish or greenish-yellow in color depending somewhat on the amount of suppuration and blood pigments present. In many cases it covers the entire area from the tip of the epiglottis downward; in others it is in patches; and in relatively few does it cover the wall of the lower part of the pharynx.

The appearance of this membrane, both grossly and microscopically is very similar to that usually seen in diphtheria. In addition, the clinical features are not unlike those in the laryngeal type of this disease: hoarseness, temperature and frequently a relatively rapid pulse. Also, throat cultures often showed that many of them harbored the typical organisms. As a result, it not infrequently happened that perplexity arose in the differential diagnosis and several times an erroneous diagnosis of diphtheria, or *vice versa*, was made.

In nearly all cases the larynx is attacked. Here the false membrane extends down into all the irregularities of this region. The reaction is usually accompanied by more or less edema surrounding the base of the epiglottis, the aryepiglottic folds and the false vocal cords. When the membrane is removed a deeply injected, hemorrhagic surface is revealed, usually showing shallow ulcerations. These are particularly likely to occur along the prominent and more rigid portions, such as the tip of the epiglottis and the edges of the vocal cords.

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[1] The term "mustard" gas is used because of the statements found on the clinical records, together with the character of the lesions which corresponds to that described in the literature.

In the trachea and larger bronchi, much the same pathology exists. There is the same sort of membrane with the injection, hemorrhage and ulceration of the underlying tissues. Here also the ulceration tends to occur on the more prominent portions, such as the mucosa over the cartilaginous rings.

In cases of longer standing the membranous exudate is less in evidence and the ulceration of the tracheal and bronchial walls is more marked. In one case (Fig. 1) the mucosa of the lower half of the trachea and of the bronchi in the region of the bifurcation was of a greenish hue and literally riddled with ulcers, one of which was 1 cm. in diameter and extended through the cartilaginous ring to the outer fibrous coat of the trachea.

The lungs are usually very voluminous, due to a marked emphysema, largely vesicular, but occasionally interstitial or bullous. Subpleural hemorrhages are frequent. There may or may not be a pleurisy depending upon the extent of the secondary infection present. There is commonly the nodular feel of a bronchopneumonia and occasionally the solidity of a massive consolidation. The cut surface is characteristic. In very mild or very early cases there may be only congestion, hemorrhages and edema of the parenchyma surrounding the bronchial tree, together with emphysema of the peripheral portions; but ordinarily the exudate described as occurring in the trachea and bronchi extends down to the finest radicles, which are not simply lined with the membrane but actually plugged. These plugs project above the cut surfaces and may be squeezed out, much like comedones. About many of these bronchioles there is a larger or smaller area of infiltration, resembling bronchopneumonia, raised, grayish or dark red (if hemorrhagic) and dry and granular in appearance. The hemorrhagic areas are prominent. Outside the pneumonic area is the vesicular emphysema.

In the older and more advanced cases necrosis is frequently present in the consolidated areas, and this becomes the more prominent feature. This occurs particularly nearer the hilus where the pneumonic areas are larger, confluent and massive, but may also be seen in the centers of the smaller discrete areas. The necrosis gives rise to abscess cavities, the larger of which have ragged, irregular walls and are filled with thin, grayish, granular, purulent and necrotic material.

Microscopically the pathology is very interesting. In the upper respiratory tract the membranous exudate lining the lumen is exactly similar to that seen in diphtheria, consisting of masses of fibrin mixed with occasional leukocytes, cellular debris and plasma. On the free surface of this exudate numerous clumps of bacteria are seen, principally diplococci. There is often no differentiation between the exudate and the mucosa of the trachea or bronchi. The epithelium is nearly everywhere absent. In a few places degenerating or necrotic cells can still be made out. The submucous tissue is infiltrated with leukocytes and is definitely edematous. There is not quite as extensive hyalinization of the fibrin, however, as one finds in a diphtherial membrane.

This type of exudate extends down into the bronchioles, where at times the lumina are completely plugged. The exudate is frequently seen attached at only one point, and here the membrane blends with the wall of the bronchiole so intimately that no differentiation is possible. The wall is markedly infiltrated with leukocytes, and this condition extends into the contiguous alveoli. In the unattached portions of the bronchial wall the epithelium may still persist. It is at the point of attachment of the fibrinopurulent membrane that the ulceration and necrosis apparently begins, and from there it extends into the deeper portions of the lung parenchyma, resulting in the formation of abscesses of the lung. In the upper portion of the tract, namely, the prominent edges of the epiglottis, vocal cords and cartilaginous rings, similar ulcerations are encountered. These ulcerations may perhaps be explained by the fact that the portions protruding into the lumen are attacked by larger quantities or by more concentrated mixtures of the poisonous gases. It is not impossible that minute droplets of the liquid gas itself are inhaled. In the lower portion of the tract the direction of the air current may determine the site of greatest injury.

The histological picture varies, depending upon the rapidity of death after the injury and consequently on the dose and concentration of the inspired gas. In several cases that came to autopsy the dose was evidently overwhelming, resulting in death from the escharotic and irritating action alone. In these rapid cases the prominent features are the edema, the profound injection of the bloodvessels and the hemorrhage. The edema generally differs from ordinary pulmonary edema in that the fluid escaping into the alveoli is considerably more albuminous, so that when coagulated it greatly resembles colloid. The fluid not only fills the vesicles around the bronchioles, but often is seen separating the cellular structure of the alveolar walls. In areas farther away from the bronchioles the albuminous fluid is deposited principally in the neighborhood of the alveolar walls, leaving clear spaces in the centers of the vesicles. Some areas show marked fibrin deposits lining the walls of the alveoli in a manner similar to the exudate seen in the bronchioles or even in the bronchi. The only difference noticeable is that there is a relative absence of leukocytic infiltration. In the centers of these alveoli there may be only a thin serum deposited or a very fine fibrinous network; sometimes the space is entirely free from exudate. In older stages the fibrin becomes hyalinized and shows an infiltration of leukocytes and the presence of degenerating desquamated epithelial cells.

Such a picture as above described helps explain the very marked dyspnea and cyanosis so frequently encountered in these cases clinically. Both the albuminous fluid around the walls of the air vesicles and the lining by dense fibrinous masses must produce a very profound interference with the normal interchange of gases in the alveoli.

Another marked feature is the injection of the bloodvessels. In many of the bronchial walls the enormously dilated capillaries present a picture of a capillary hemangioma. Also the extensive hemorrhage, which is so commonly seen in the alveoli surrounding the bronchioles, gives a picture, with the low power of the microscope, which resembles a cavernous hemangioma of the liver. The capillaries of the alveolar walls are dilated and tortuous. It requires very little imagination to visualize the processes by which the extensive hemorrhages occur.

The histology of the peripheral portions of the lungs shows little except vesicular emphysema. In later stages, with advanced pneumonic involvement, pleurisy may be present.

In the older cases, that is, in cases which die of the secondary infection rather than from the direct effects of the gas, there is a picture of bronchopneumonia. But even here the marked edema and hemorrhage, along with the peculiar deposits of fibrin, make the diagnoses fairly easy. Areas of necrosis are now present. These apparently begin in the walls of the bronchioles and extend centripetally, forming occasionally large abscesses filled with pus and necrotic debris. Around these necrotic areas the alveolar walls often show thickening due to fibrosis and infiltration, with round cells and polymorphonuclears. The alveoli contain dense masses of precipitated serum or fibrin in various stages of organization. Some show only a slight infiltration with leukocytes; others show fibroblasts from the alveolar walls invading the masses; still others show fairly well-advanced organization of the exudate. These areas are generally small and surround the bronchioles in the regions where the abscesses are apparent. The picture is unlike the ordinary types of organization pneumonias, in that the areas of necrosis and the abscesses are more common. Some of the bronchioles also show organization of the exudate, so that if the case should go on to healing the bronchioles would probably become organized into fibrous cords.

No changes were evident in the bronchial walls that could be taken for bronchiectases. However, the various lesions seen in the bronchi and bronchioles might lead to great weakening and dilatation if the patient should go on to recovery.

Case No.	Hosp. No.	Days after gassing.	Skin and eyes.	Larynx.	Trachea.	Bronchi.	Bronchioles.	Lung.	Clinical data.	Cause of death.
1	25-27	18	Extensive burns; severe conjunctivitis	False membrane; hemorrhage; ulceration	False membrane; hemorrhage; ulceration	False membrane; hemorrhage; ulceration	Plugged with thick exudate	Small patches of consolidation	....	Skin, burns of, extensive.
2	25-32	6	Severe second degree burn of face, neck, buttocks, thighs; severe conjunctivitis	Heavy false membrane; surface ulcerated; edema of glottis	Heavy false membrane; lower part hemorrhagic	Thin fibrinopurulent membrane	Many occluded by plugs of fibrinopurulent membrane	Edema; small patches of consolidation	Cyanosis; severe cough; pain in chest; albuminuria	Acute fibrinopurulent tracheobronchitis.
3	25-38	6	Skin mild, not extensive burns; eyes inflamed	Purulent exudate; hemorrhagic	Injected; thin fibrinopurulent exudate	Thick fibrinopurulent exudate	Many completely plugged with thick exudate	Marked edema; moderate patches of consolidation	Fever; eyes swollen; pain in chest; delirium	Acute hemorrhagic and purulent tracheobronchitis.
4	25-39	6	Mild skin burns	Thick purulent exudate; hemorrhage; ulceration	Thick purulent exudate; hemorrhage; ulceration	Thick purulent exudate; hemorrhage; ulceration	Many completely plugged with thick exudate	Emphysematous; small nodules of consolidation	Fever; dyspnea	Acute ulcerative and suppurative tracheobronchitis.
5	25-40	20	....	Congested; thin layer of purulent exudate	....	Congestion; fibrinopurulent exudate	Congested fibrinopurulent plugs	Small patches of bronchopneumonia; edema	Temperature; swelling of eyes; bronchitis and pulmonary edema	Acute suppurative laryngitis and bronchitis; bronchopneumonia.
6	25-45	29	Large superficial skin burns; eyes congested and lids ulcerated	Injected; thickened; yellow thick purulent exudate; ulceration	Injected mucosa thickened	Fibrinopurulent membrane	....	Diffuse bilateral bronchopneumonia; edema; emphysema	Cyanosis; dyspnea; conjunctivitis; signs of bronchopneumonia	Acute suppurative tracheobronchitis and ulcerative laryngitis; bronchopneumonia.
7	25-48	17	Severe burns of genitals; eyes acutely inflamed	Ulceration; hemorrhage	Thick fibrinopurulent membrane; hemorrhage; ulceration	Thick fibrinopurulent membrane; hemorrhage; ulceration	....	Diffuse bronchopneumonia; emphysema marked	Fever; cyanosis and dyspnea	Acute suppurative and ulcerative tracheobronchitis; bronchopneumonia.
8	25-50	12	Severe burns of face; severe conjunctivitis	Congestion; hemorrhage; thin yellow fibrinopurulent exudate	....	....	....	Bronchopneumonia, diffuse; pulmonary necrosis; edema marked	Profuse expectoration; diffuse bronchitis; membrane on the soft palate	Bronchopneumonia and acute purulent tracheobronchitis.
9	25-56	10	Severe conjunctivitis	....	Thin yellow exudate; hemorrhage; ulceration	Thin yellow exudate; hemorrhage; ulceration	....	Bronchopneumonia, diffuse emphysema and edema marked	Fever; cyanosis; dyspnea; diffuse bronchitis	Acute suppurative tracheobronchitis and bronchopneumonia.
10	26-16	3	Mild skin burns; severe hemorrhagic conjunctivitis	Hemorrhage; ulceration; purulent exudate; edema of glottis	Hemorrhage; ulceration; purulent exudate	Hemorrhage; fibrinopurulent exudate	Many completely plugged with thick exudate	Early bronchopneumonia; marked emphysema	Coma; dyspnea; cyanosis; temperature and rapid pulse	Acute hemorrhagic and suppurative tracheobronchitis and edema of glottis; bronchopneumonia.

11	26–18	4	Burn of genitalia; severe conjunctivitis	Hemorrhage; edema; plastic exudate	Hemorrhage; edema; plastic exudate	Hemorrhage; edema; plastic exudate	Many completely plugged with exudate	Early bronchopneumonia; marked emphysema	Cyanosis; dyspnea	Acute hemorrhagic and suppurative tracheobronchitis; bronchopneumonia.
12	26–26	13	....	....	....	Left has plastic exudate	....	....	Temperature; dyspnea; albumin and casts	Acute fibrinous bronchitis and edema of lungs.
13	26–30	17	Severe second degree burns; severe conjunctivitis	....	....	Congested; moderate purulent exudate	Congested	....	Burns of skin only	Severe skin burns.
14	26–44	5	Severe conjunctivitis	Fibrinopurulent exudate	Congestion and fibrinopurulent exudate	Congestion and fibrinopurulent exudate	Purulent exudate	Massive bronchopneumonia	Cyanosis; dyspnea	Bronchopneumonia; suppurative bronchitis and tracheitis.
15	26–46	6	Congestion and hemorrhage in the conjunctivæ	Fibrinopurulent exudate	Fibrinopurulent exudate	Fibrinopurulent exudate	Many plugged with heavy fibrinopurulent exudate	Moderate bronchopneumonia; edema	Dyspnea; conjunctivitis	Acute fibrinopurulent tracheobronchitis; bronchopneumonia.
16	26–52	10	Second degree burns of scrotum; severe conjunctivitis	Hemorrhage; ulceration; fibrinopurulent exudate	Hemorrhage; ulceration; fibrinopurulent exudate	Hemorrhage; ulceration; fibrinopurulent exudate	Purulent exudate	Bronchopneumonia	Fever; sore throat; signs of pneumonia	Acute suppurative ulcerated tracheobronchitis; bronchopneumonia.
17	26–56	9	Slight skin burns; marked acute conjunctivitis	Thick exudate; vocal cords edematous and ulcerated	Heavy fibrinopurulent exudate	Casts of bronchi in pseudomembrane	Plugged with thick exudate	Early bronchopneumonia	Dyspnea; cyanosis; fever; signs of pneumonia	Diphtheria; edema of glottis; acute suppurative and ulcerative tracheobronchitis; bronchopneumonia.
18	26–59	25	Moderate skin burns; ulceration of eyelids	Plastic exudate; ulceration	Marked fibrinopurulent exudate	Very marked fibrinopurulent exudate	Many completely plugged with thick exudate	Marked bronchopneumonia	Fever; dyspnea; cough	Acute ulcerative and membranous tracheobronchitis; bronchopneumonia.
19	26–62 A.	21	Moderate skin burns; ulceration of lids	Fibrinopurulent pseudomembrane	Hemorrhage; ulceration; fibrinopurulent exudate	....	Pus	Advanced bronchopneumonia; necrosis (early)	....	Bronchopneumonia; ulcerative and membranous tracheobronchitis.
20	26–74	17	....	Fibrinopurulent pseudomembrane	Fibrinopurulent pseudomembrane	Pseudomembrane and pus	Many plugged with thick exudate	Early bronchopneumonia; edema; emphysema	Fever; hoarseness; cough; pain in chest; dyspnea	Acute suppurative tracheobronchitis; bronchopneumonia.
21	26–1	11	Severe skin burns of face and neck; eyes burned	....	....	....	....	....	....	Cellulitis of face and head following burns in these regions.
22	49–32	7	Severe skin burns; eyes injected	Thick fibrinopurulent exudate; ulceration; hemorrhage	Thick plastic exudate; ulceration; hemorrhage	Thick plastic exudate; ulceration; hemorrhage	Many plugged with thick exudate	Edema	Dyspnea; pain in chest; weak pulse	Acute fibrinopurulent tracheobronchitis.
23	49–31	4	Severe, not extensive burns; purulent conjunctivitis	Thick fibrinopurulent exudate; ulceration	Thick fibrinopurulent exudate; ulceration	Thick fibrinopurulent exudate; ulceration	Pus	Hemorrhage	Cough; dyspnea; cyanosis	Acute suppurative and ulcerative tracheobronchitis.

Case No.	Hosp. No.	Days after gassing.	Skin and eyes.	Larynx.	Trachea.	Bronchi.	Bronchioles.	Lung.	Clinical data.	Cause of death.
24	49–36	5	Slight burns of face; eyes swollen	Greenish-yellow fibrinopurulent exudate	Greenish-yellow fibrinopurulent exudate	Greenish-yellow fibrinopurulent exudate	Plugged with similar exudate	Bronchopneumonia moderate; edema	Fever; delirium; eyes swollen	Acute suppurative and ulcerative tracheobronchitis; bronchopneumonia.
25	49–51	7	....	....	Fibrinopurulent pseudomembrane	....	Plugged with similar exudate	Bronchopneumonia; marked edema; emphysema	Fever	Acute fibrinopurulent tracheobronchitis and bronchopneumonia.
26	49–67	25	Mild burns of head, chest, arms; conjunctivitis	Fibrinopurulent exudate	Fibrinopurulent exudate	....	Many plugged with similar exudate	Bronchopneumonia; marked emphysema	....	Acute fibrinopurulent tracheobronchitis and bronchopneumonia.
27	56–2	6	....	....	Congested	Hemorrhagic	Hemorrhagic	Marked edema	....	Acute hemorrhagic bronchitis; edema of lungs.
28	56–7	?	....	Fibrinopurulent membrane; congestion; edema	Fibrinopurulent membrane; congestion; edema	Congestion; edema	Congestion; edema	Very marked edema	....	Edema of glottis.
29	56–14	16	....	....	....	....	....	Bronchopneumonia	....	Bronchopneumonia.
30	56–19	4	Skin of face slightly burned; corneal opacity	Fibrinopurulent exudate; ulceration; hemorrhage	Fibrinopurulent exudate; ulceration; hemorrhage	....	Many plugged with similar membrane	Emphysema	....	Acute suppurative and ulcerative tracheobronchitis.
31	56–30	18	Few mild burns; conjunctivitis	Thin fibrinopurulent exudate and ulceration; edema of glottis	....	....	Many plugged with similar exudate	Early bronchopneumonia	Fever	Suppurative tracheobronchitis; bronchopneumonia.
32	56–44	35	Conjunctivitis	Pseudomembrane (gas and diphtheria); edema of glottis	Fibrinopurulent membrane	....	....	Hemorrhage	Fever; diphtheria	Septicemia; diphtheria; acute fibrinopurulent tracheobronchitis.
33	56–57	34	Conjunctivitis	Fibrinopurulent pseudomembrane	....	....	Pus	Massive bronchopneumonia	Violent cough, burning in chest; aphonia; nausea and vomiting	Acute fibrinopurulent tracheobronchitis; bronchopneumonia.
34	56–	70	Acute conjunctivitis	....	Numerous deep ulcerations	....	Fibrinopurulent plugs and necrosis	Massive bronchopneumonia; abscess formation due to necrosis	....	Gangrenous and ulcerative tracheobronchitis; lung abscess; bronchopneumonia.
35	19–1	?	Slight burns of face; congested conjunctivæ	....	....	Injected	Pus	Bronchopneumonia; emphysema marked	....	Bronchopneumonia.

In one of the cases studied the condition had gone on for several months and yet no bronchiectases were apparent in the lungs. In the cases of influenza-pneumonias studied in this center, bronchiectatic changes were relatively common and were apparent in lesions of much shorter duration. It is therefore quite likely that the lung pathology following influenza is more susceptible to the development of bronchiectasis than that following gas inhalation.

The pathogenesis of these lesions cannot be completely worked out from the material obtained at this center, because no cases came to autopsy under four or five days after exposure. However, by correlating the findings, and by making a composite picture of all the lesions encountered in the various stages of the disease, one might visualize the processes of reaction about as follows:

As the irritating gas is inspired, some of the exposed cells may become immediately necrosed. The capillaries nearest the surfaces become engorged. This is true also in the smallest bronchioles and perhaps in the alveoli themselves. The irritation causes an exudate consisting of a moderate quantity of heavy albuminous fluid in contradistinction to the huge quantities of thin fluid poured out in cases of phosgene inhalation. Later, cellular elements appear in the exudate along with desquamated epithelial cells. Some of the fibrinogen is converted into fibrin, which forms a lining not only along the upper tube of the respiratory tract but also may extend down into the terminal bronchioles and air cells. Depending upon the amount of irritation, the exudate, which is now fibrinopurulent in character, may increase in thickness until it may produce a layer 3 or 4 mm. in depth in the larynx, trachea and bronchi. There is at the same time a marked edema and congestion of the loose subepithelial cellular tissues. In proportion to the amount of congestion and the extent of the necrosis produced will be the extent of the ulceration along the larynx, trachea and bronchi and the hemorrhages in the lung parenchyma. The amount of exudate in the smaller bronchioles may become so abundant as to completely plug the lumina. This obstruction of some of the bronchioles will result in the compensatory emphysema of other portions of the lung.

The upper respiratory tract is constantly exposed to infection, which will soon result in a superimposed inflammatory reaction, due to the bacterial invasion. This infective process will gradually descend into the bronchioles, owing to the lowering in the resistance of the tissues. It is at this time that polymorphonuclear infiltration may become very abundant and produce miliary or submiliary nodules, which finally may become confluent. Because the gas is in the greatest concentration in the upper portion of the respiratory tract the greatest pathological changes will be produced around the hilus. If the necrosis is very extensive, very profound ulcerations may develop in the trachea and larynx, which may almost penetrate the walls. In the lung parenchyma the necrosis will gradually develop into areas of hemorrhage and into abscess formation after the necrotic area becomes secondarily infected with bacteria.

If the patient receives severe burns in the respiratory tract but is still able to live for any length of time, for example, several months, then the resulting lesions will present the large areas of consolidation, pneumonic in character, through which will be scattered large or small areas of necrosis, with abscess formation. The attempt at healing will manifest itself by the definite evidences of organization of the exudate and the fibrosis, as previously described.

The following brief protocols are presented to illustrate the conditions found at autopsy in several cases of gas inhalation in which death occurred from five days to over two months after the injury. The first case is of a very early type while the last is an old and very advanced stage of the disease. Only the important data are given; the negative findings are omitted.

CASE REPORTS.

CASE I.—Autopsy 26-16. E. B. P., Sergeant, Co. H, 306 Infantry, No. 1702538. Aged twenty-two years, white. Died September 28, 1918, at 6 A.M., at Base Hospital 26. Autopsied September 28, 1918, at 10 A.M. Capt. Moses Barron, M.C., pathologist.

"*Clinical Data.* This case is that of a young man admitted to Base Hospital 26 at 6 P. M., September 27, 1918, from Hospital Train No. 63, with a diagnosis of gas, deleterious, absorption of, inhalation and surface contact. Temperature was 98°, pulse 156, respiration 20. The field medical card had been lost in transfer to the train. History obtained stated that he had been gassed three days previously. He was comatose, markedly cyanotic and breathed with great difficulty. The throat was reddened and swollen. The eyes were closed with purulent exudate. There were rales throughout the chest, with bronchial breathing suggesting consolidation. Diagnosis (addition) was made of bronchopneumonia, left lower lobe. September 28, temperature was 99°, pulse 108, respiration 16. Death occurred at 6 A.M.

"*External Appearances.* There is purulent exudate on the conjunctivæ of both eyes, with accumulation at the margins of the upper and lower lids. Small hemorrhages are present on the ocular conjunctivæ laterally to the corneæ. There is a vesicle around the external meatus of the urethra, 2 x 3 cm., and one on the anterior surface of the tibia, 1 cm. in diameter, 7 cm. below the patella. There is another vesicle, 2 cm. in diameter, 1 cm. below the internal malleolus, left.

"*Organs of the Mouth and Neck.* On opening the trachea and larynx there is found marked edema of the mucosa and submucosa. Pin-point hemorrhages, with minute ulcerations, are scattered over the entire epithelium. A purulent exudate covers the surface, very marked over the vocal cords and at the base of the epiglottis. This is firmly adherent to the epithelium. The vocal cords are greatly thickened and the glottis appears almost completely closed through the approximation of the swollen tissues covered by the exudate.

"Lungs: On opening the bronchi they are found to be almost completely filled with tenacious masses of exudate. In the smaller bronchioles these assume a pseudomembranous character. They extend into the still smaller bronchioles as solid plugs, completely closing the lumina. On stripping the exudate the epithelium throughout shows pin-point hemorrhages, with minute ulcerations.

"Left: The lower lobe is large and voluminous. The lower half is feathery. It contains several irregular collapsed areas, reddish brown in color, in contrast to the grayish pink of the rest of the lung. There are firm, irregular masses present, which on section are reddish brown in color and contain grayish areas, 1 to 5 mm. in diameter, from the centers of which pus escapes from the bronchioles. The lower margin of the upper lobe is firm but crepitates slightly. On section, quantities of faintly turbid, blood-tinged fluid escape.

"Right: The right lung has only two lobes. The lower lobe is voluminous, light and feathery. The lower surface of the upper lobe shows numerous air vesicles varying from pin-point size to 2 mm. in diameter, situated along the interlobular septa. On section, quantities of pus escape from the large bronchioles.

"*Anatomical Diagnosis.* Edema of glottis; acute suppurative and ulcerative tracheobronchitis; beginning bronchopneumonia; edema of lungs; acute vesicular and interstitial emphysema; edema and congestion of the brain; congestion of the kidneys; gas burns of the conjunctivæ and skin.

"*Probable Cause of Death.* Acute suppurative tracheobronchitis, with beginning bronchopneumonia and edema of the glottis, following gas inhalation."

Microscopic Study (Section 46). The bronchioles are lined with a fibrinopurulent exudate. Some bronchioles are completely plugged. The plugs present a denser infiltration with leukocytes. The mucosa is nearly everywhere absent and the walls are infiltrated with polymorphonuclears. The capillaries are intensely injected. The alveolar walls immediately surrounding the bronchioles also show this injection of the capillaries, but the air vesicles contain relatively very little exudate. A few of the bronchioles are surrounded by a narrow zone of alveoli filled with polymorphonuclear leukocytes and some fibrin. There are small patches of edema in which the albuminous precipitate is very dense, resembling colloid.

Another section of the same lung shows an almost similar picture, but the purulent exudate in the alveoli is somewhat more marked.

CASE II.—Autopsy 25-32. W. B., Corporal, Co. F, 26 Infantry, No. 284685. Aged twenty-three years, white. Died October 14, 1918, at 2.45 A.M. Autopsied October 14, 1918, at 11 A.M. Capt. Moses Barron, M.C., pathologist.

"*Clinical Data.* This is the case of a man who was admitted to Base Hospital No. 25 on October 10, 1918, with extensive skin burns (second degree) over the face, neck, buttocks and thighs, due to mustard-gas contact. Inhalation of the same gas caused a severe inflammatory condition of the respiratory passages. Upon admission the patient was cyanotic, coughed frequently and complained of pains in the chest. Urinalysis showed albumin in the urine and hyalin and granular casts. The patient died at 2.45 A.M. on October 14, 1918.

"Lungs: The lungs and organs of the neck are removed *en masse.* The pyriform sinuses are covered by a thick, fibrinopurulent membrane, which is firm and adherent. The epiglottis is thickened and covered by a similar membrane. The entire larynx, including the vocal cords, presents a thick, shaggy membranous exudate, which, when removed, leaves a congested, necrotic and somewhat ulcerated surface. Portions of the exudate extend for a short distance into the trachea. Farther down into the trachea the mucosa is hemorrhagic, purplish red in color and covered by a thin hemorrhagic and purulent exudate, which becomes more marked in the bronchi and bronchioles where it almost occludes the lumina. On section of the lungs the cut surfaces are mottled, dark brown and red, with yellowish plugs completely filling some of the small bronchioles. On pressure large quantities of frothy fluid flow from the cut surfaces. The organs crepitate only slightly. Some of the bronchioles are surrounded by small grayish yellow, firm areas. The pleura is covered by a thin layer of fibrinopurulent exudate.

"*Anatomical Diagnosis.* Acute fibrinopurulent, hemorrhagic and ulcerative tracheobronchitis, with moderate edema of the glottis; early bronchopneumonia, with edema and congestion of the lungs; acute fibrinopurulent pleuritis; diffuse colloid thyroid; superficial burns of the skin from poisonous gas; mild acute diffuse nephritis.

"*Probable Cause of Death.* Acute fibrinopurulent and hemorrhagic tracheobronchitis, with edema of the lungs and partial edema of the glottis following inhalation of poisonous gas."

Microscopic Study (Section 426). The bloodvessels throughout the section are dilated and engorged. The bronchioles are plugged with fibrinopurulent exudate. In two bronchioles these plugs are seen to be attached to the wall at one side, at which point the mucosa is destroyed and the wall is edematous and extensively infiltrated with leukocytes. Remnants of mucous membrane are to be seen on the remainder of the bronchial wall. The capillaries in the wall are markedly engorged with blood. About the bronchioles there is extensive hemorrhage into the alveoli. Patches of hemorrhage alternating with emphysematous areas are scattered throughout the parenchyma. In some portions of the section the alveoli around the bronchioles are filled with a purulent exudate.

Case III.—Autopsy 26-62. A. R. B., Private, Co. I, 61 Infantry, No. 2253041. Aged twenty-two years, white. Died October 31, 1918, at Base Hospital 26. Autopsied November 1, 1918. Lieut. Oliver C. Melson, M.C., pathologist.

"*Clinical Data.* This case is that of a man who was admitted to Base Hospital 26, October 12, 1918, with a gunshot wound of the right lumbar region. He was suffering from absorption of gas, deleterious, mustard, by inhalation and contact. (Clinical record is not available.) Death occurred October 31, 1918.

"*External Appearances.* . . . There are superficial ulcerations of the ears, eyes, nose and mouth. The skin of the right hand and forearm, both legs, both buttocks and back is pigmented. There are multiple superficial burns of the skin of the right arm, extending from 6 cm. above the elbow to 5 cm. below it on the lateral and flexor surface; on the flexor surface of the right forearm, 4 cm. in diameter; on the left forearm an area, 1 cm. in diameter, 2 cm. above the wrist-joint on the extensor surface, extending 2 cm. upward and inward; and also a smaller, more superficial burn, 5 mm. in diameter. The skin over practically the entire back is involved in superficial burns. . . . The posterior and inner surfaces of both legs, from the upper third of the thigh to 6 cm. below the knee-joint on the left, are involved in superficial burns as well as the anterior surface of the left knee-joint. There are also superficial burns over the external genitalia. There is a debrided wound, partially closed by silkworm sutures and drained by tubes, which extends from the midline (of the back) to the level of the third sacral segment and downward to the left trochanter. The mesial portion of the wound connects with the coccyx, which is fractured. . . ."

"*Organs of the Neck.* The mucous membrane of the trachea and larynx is covered by fibrinopurulent exudate, which is very adherent, appearing as a pseudomembrane. Near the bifurcation of the trachea the mucous membrane is hemorrhagic, with minute ulcerations scattered over the surface.

"Right Lung: The right lung is nodular and crepitant. The pleura is thickened and covered by many firm fibrous adhesions. The cut surface is dark red, moist and studded with irregular round raised areas, reddish in color. From the centers of these areas, yellow, purulent material can be expressed on pressure. Many are soft and necrotic, with a very foul odor.

"Left Lung: The left lung is nodular and crepitant. It is salmon colored and mottled with anthracotic pigment. The lower lobe is covered by shaggy, fibrous adhesions. At the apex of the upper lobe is a firm, grayish, non-aircontaining area, 5 cm. in diameter, which is granular to the feel and on pressure exudes large quantities of yellow purulent material. This area is sharply demarcated from the surrounding tissue. The remainder of the lung corresponds to the right in description, except that the nodules are fewer in number. The bronchi contain a considerable quantity of frothy bloody fluid. The mucous membrane is markedly injected.

Anatomical Diagnosis. Advanced bilateral bronchopneumonia, with necrosis and abscess formation; acute hemorrhagic, suppurative and ulcerative tracheobronchitis (due to gas inhalation); multiple superficial skin burns; gunshot wound of the left buttock, with compound comminuted fracture of the coccyx; chronic adhesive pleuritis.

"*Probable Cause of Death.* Acute suppurative and ulcerative tracheobronchitis and bronchopneumonia."

Case IV.—Autopsy 56–68. A. R. M., Private, Co. H., 312 Infantry, No. 3754421. Aged twenty-one years, white. Died January 3, 1919, at 3.45 p.m., at Base Hospital 56. Autopsied January 4, 1919, at 9.30 a.m. First Lieut. George W. Covey, M.C., pathologist.

"*Clinical Data.* This is the case of a man who was admitted to Base Hospital 26 on October 24, 1918, with the history of having been exposed to mustard gas on October 18. There were no skin burns, but the eyes were much inflamed. Examination showed the patient to be quite cyanotic, with marked conjunctivitis, accompanied by purulent discharge and ciliary injection. The pharynx was much injected; pulse good; heart negative; lungs showed many whistling rales throughout, with crackling rales in both bases most marked in the left posteriorly. No definite consolidation. Temperature 102°. October 27, smear negative for B. diphtheria. Dulness and suppression of breath sounds in areas in the right axilla and the right base posteriorly. November 25 he was much improved; still much semipurulent expectoration and cough; chest full of moist and sonorous rales. Heart rapid. Persistent afternoon temperature of 100°. November 30 the throat culture was positive for diphtheria and 10,000 units of diphtheria antitoxin given. He was transferred to Base Hospital 56 on December 1, with very marked membrane on both tonsils. Marked hoarseness. Given 30,000 units of diphtheria antitoxin at 3 p.m. · December 3 was given 20,000 units of antitoxin at 9.10 p.m. December 4 the examination of the chest showed marked bronchial breathing all over the lungs, with many rales of all characters. Diagnosis: acute diffuse bronchopneumonia, bilateral, secondary to absorption of mustard gas; diphtheria, pharyngeal and tonsillar. He was given a total of 120,000 units of antitoxin. December 10 the patient had an attack of dyspnea lasting a few minutes. Examination showed respiration of asthmatic type, at the bases a few mucous rales, with areas of consolidation. There was a partial paralysis of the palate. December 17 his condition was about the same; sputum negative for tubercles. December 23 the patient had consolidation of right base of bronchopneumonic type. Quite dyspneic. January 3, 1919, his condition was worse;

unable to take nourishment; bubbling rales throughout lungs. Died at 4 P.M., January 3.

"Pleural Cavities: The left pleural cavity has a strong band of adhesions at the apex. There is no excess of fluid. The right also has a strong band of adhesions at the apex and no increase in fluid.

"Lungs and Organs of Neck: The organs of the neck and the lungs are removed *en masse*. The esophagus is normal. The tonsils, pharynx and upper portion of the larynx are normal. Just below the posterior extremity of each vocal cord there is an opening, about 5 mm. in diameter, leading into a cavity which extends into the laryngeal wall for a distance of about 1 cm. Pus can be expressed from these cavities; otherwise the larynx and upper 5 cm. of the trachea are normal. Beginning about 5 cm. below the larynx and continuing downward throughout the trachea and bronchi the mucosa is dark greenish in color, hemorrhagic and covered with pus. About 5 cm. above the bifurcation there is an ulcer with undermined edges, extending through the mucosa and through a cartilaginous ring to the outer coat of the trachea. It measures 1 cm. in diameter. From this point downward there are similar ulcerations becoming more and more numerous (Fig. 1).

"The left lung is voluminous, heavier than normal. There is a scar at the apex. Numerous hemorrhages are present beneath the pleura. There is marked vesicular emphysema. The cut surface of the upper lobe reveals a group of calcified nodules beneath the scar. The color is normal. Large quantities of pus are expressed from the bronchi and plugs of thick white exudate are expressed from the smaller bronchi and bronchioles. The cut surface of the lower lobe is dark red in color and practically every bronchus contains a plug of exudate which projects above the surface. Frothy bloody fluid exudes from the parenchyma.

"The right lung is heavy, large, firm, with marked vesicular emphysema and numerous hemorrhages beneath the pleura. The pleura is covered by a fibrinopurulent exudate. The cut surfaces of the upper and lower lobes are similar and as follows: Several large, ragged, irregular abscess cavities filled with thin grayish, granular pus, are scattered through the central portions of these lobes from the apex to the base (Fig. 2). They vary from a few millimeters to two or more centimeters in diameter. The central portion of both lobes is an airless, gray, granular mass—a central pneumonia. Toward the pleura the pneumonic areas become more discrete and are seen as gray, raised, granular areas varying from 3 or 4 mm. to 1 cm. or more in diameter, quite definitely circumscribed. In the center of each is a bronchiole from which a plug of exudate can be expressed. Occasionally the center of a larger discrete area is seen to be necrotic, with a small abscess cavity (Figs. 1 and 2). The parenchyma intervening between the pneumonic areas is dark red in color and emphysematous, with areas of hemorrhage. Near the hilus are scattered areas showing interlacing, firm yellowish streaks suggesting organization.

"*Anatomical Diagnosis.* Marked gangrenous and ulcerative tracheobronchitis; marked fibrinopurulent bronchitis of smaller bronchi; massive bronchopneumonia, right, with extensive necrosis and abscess formation; healed pulmonary tuberculosis; right-sided fibrinopurulent pleuritis; chronic adhesive pleuritis; marked vesicular emphysema.

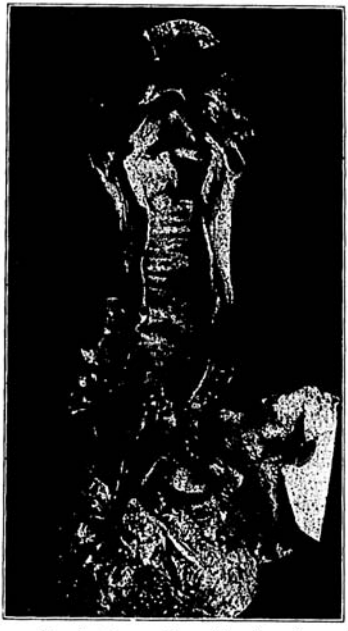

FIG. 1.—Larynx and trachea two months and ten days after gassing (Aut. 55-68, Case IV in text). Note extensive ulcerations, most marked at the bifurcation. The large transversely placed ulcer in the lower part of the trachea perforated through a cartilaginous ring.

"*Probable Cause of Death.* Gangrenous and ulcerative tracheobronchitis; bronchopneumonia, with abscess formation—following inhalation of poisonous gases."

Microscopic Study (Slide 449). The striking feature of the section is a small bronchus dilated and filled with pus cells. In the center of this mass is a group of vegetable cells and spirals. The wall of the bronchus is only faintly visible, being infiltrated with polymorphonuclear leukocytes. The mucosa is entirely absent. The capillaries are intensely injected and dilated. In two places the wall is completely necrosed, and this necrosis extends for some distance into the parenchyma of the lung. About the bronchus and throughout the section there is thickening of the alveolar walls, which are infiltrated with polymorphonuclears and show a large increase of connective tissue. The alveoli are filled with fibrin and heavy precipitated serum through which are scattered a few cells. Fibroblasts are seen penetrating the exudate in numerous instances, and some alveoli are completely fibrosed.

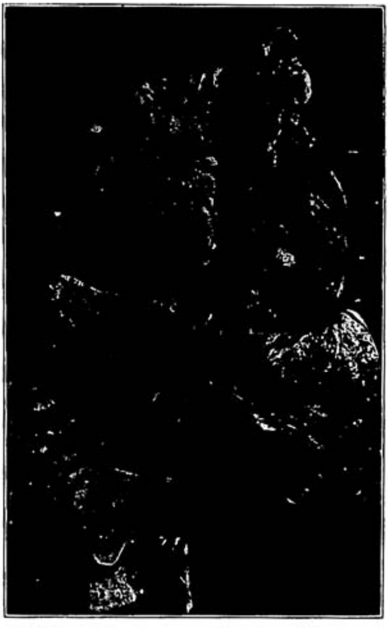

FIG. 2.—Lung from same case as Fig. 1. (The trachea and larynx are lying back of the lung, with the epiglottis and base of tongue showing just beneath the base of lung). Note the numerous areas of consolidation scattered throughout the cut surfaces. In the centers of many of these the emptied lumina of the bronchioles may be seen. Note the ragged areas of necrosis and abscess cavities.

DISCUSSION. Case I died the day after admission, and, allowing one day for transportation from the field, about five days after gassing. Here are seen, as the outstanding features, edema, congestion, hemorrhages and very small ulcerations, with thin fibrinopurulent exudate in the upper respiratory tract. In the lower air passages one finds much the same picture with a more tenacious exudate which almost completely plugs many bronchioles. The parenchyma shows congestion, edema, emphysema, areas of atelectasis and very small bronchopneumonic areas.

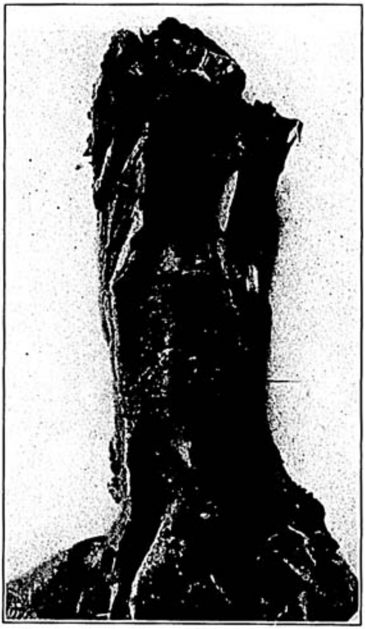

FIG. 3.—Larynx and trachea from a case of mustard-gas inhalation. Note extensive edema of aryepiglottic folds especially the right; thick, shaggy membrane covering the larynx and vocal cords; membrane in patches on the wall of the trachea and bronchi; small ulceration of the wall near the bifurcation.

Case II died about six days after gassing. The exudate in this case is much more abundant than in Case I, and is shaggy and membranous. The ulcers in the trachea are a little more prominent. There is already a pleurisy present.

Case III died twenty days after gassing. The air passages show a marked pseudomembrane, and, upon its removal, a hemorrhagic and ulcerated surface. The lungs showed an advanced bronchopneumonia, with beginning necrosis and abscess formation in the center of some of the pneumonic areas.

Case IV died two months and ten days after being gassed. The air passages, trachea and bronchi show no membrane, but instead show marked necrosis of the mucosa, with large, deep ulcerations extending nearly through the tracheal wall. The lungs show extensive necrosis and abscess formation, accompanying a massive bronchopneumonia. The attempt at healing is shown by the organization of the exudate. Many alveolar walls are thickened and some alveoli are completely fibrosed. Strange to say, much albuminous deposit and fibrin are still in evidence in the air cells. Unfortunately, this case was complicated by clinical diphtheria, but most probably this complication did not materially change the lesions found at autopsy. Only one finding brings up a question of etiology: the evidences of the aspiration pneumonia as revealed by food particles lying imbedded in the purulent exudate within the small radicles of the bronchi. Was the aspiration of the material due to the par-

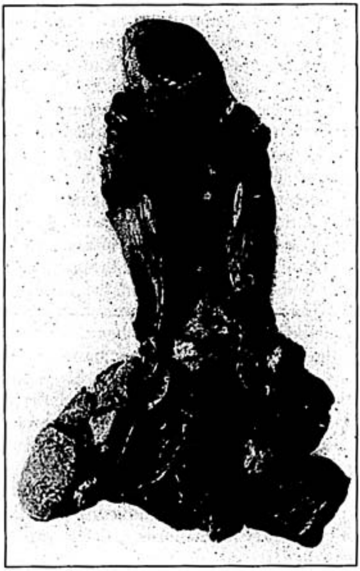

FIG. 4.—Larynx and trachea from case of mustard-gas inhalation. Note thick membrane covering epiglottis, obscuring the vocal cords and extending in patches down the trachea; thick membrane on the walls of the primary bronchi; small ulcerations of tracheal wall near the bifurcation.

alysis following the diphtheria or to the deep ulcers in the trachea opposite the esophagus? The abscess formation might also have been augmented by the aspiration of the foreign material.

To recapitulate: Stage one, as represented by the first two cases, is characterized by mild edema, hemorrhage, beginning ulceration, early fibrinous deposit, emphysema and very early bronchopneumonia. Stage two (Case III) by a marked fibrinopurulent pseudomembrane, more extensive ulceration, emphysema, advanced bronchopneumonia and beginning necrosis. Stage three (Case IV) by ulceration, necrosis and abscess formation, with massive bronchopneumonia. The attempts at healing are revealed by the organization and fibrosis.

It is interesting to speculate on the outcome of a case similar to the fourth should such a case go on to recovery or if the lesions in the trachea should continue to progress. The tracheal ulcerations might easily perforate the wall, resulting in mediastinal abscess. Those in the bronchi near the bifurcation might ulcerate through and through and perforate the aorta. When such ulcers heal, contractures are sure to obtain. These contractures may result in traction diverticulæ of the esophagus. In the parenchyma, organization would occur and result in disseminated patches of fibrosis or even in extensive fibrosis of the lungs resembling healed tuberculous lesions. Some of the bronchioles might be transformed into fibrous cords through the organization of the exudate.

In milder involvement the walls only might go on to a fibrosis of a greater or lesser degree, which would result clinically in a chronic bronchitis. Upon the extent of the injury to the bronchial tree will depend the intensity of the clinical symptoms of convalescent and recovered cases, as manifested by the chronic bronchitis and emphysema. From what has been said above, many cases will undoubtedly present grave clinical difficulties in the differential diagnosis from pulmonary tuberculosis.

CLIMACTERIC HYPERTENSION: A STUDY OF HIGH BLOOD-PRESSURE DURING AND FOLLOWING THE MENOPAUSE.

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In this paper it is my purpose to describe a type of high blood-pressure developing in women at the time of the menopause and possibly the result of it, in which there is no discernible arteriosclerosis, at least, for some years after its onset, no renal involve-